REMARKS

Applicants respectfully request reconsideration and reexamination of the present application in light of the amendments and the remarks below.

Claims 1-24 are pending in this application. Claims 4-7, 9-11, and 13-24 have been amended. These claim amendments are made to clarify the subject matter therein. Therefore, these amendments are submitted in order to place the claims in condition for allowance, and do not disclaim any subject matter to which the Applicants are entitled.

Rejection Under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 1, 9, 10, 11, 13, 14, 15, 18, and 21-24 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention (Paper No. 7, pages 3-5). Applicants respectfully traverse this rejection.

The Examiner stated that claim 1 recites the limitation "Process for preparing CCDC semihydrochloride according to claim 1," and there is insufficient antecedent basis for this limitation in the claim. Claim 1 is not a process claim, it is directed to a compound, that is, semi-hydrochloride of 8-cyano-1-cyclopropyl-7-(1S,6S-2,8-diazabicyclo[4.3.0]nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid. A clarification of the rejection is requested.

The Examiner stated that the term "medicament" in claims 9, 10, and 16-21, is indefinite. The claims have been amended as suggested by the Examiner.

The Examiner stated that the phrase "characterized in that" in claims 9, 16, 17, and 18 is indefinite. The claims have been amended accordingly.

The Examiner stated that claims 13, 14, and 15 recite the limitation "Process for preparing CCDC semihydrochloride according to Claim 2," "Process for preparing CCDC semihydrochloride according to Claim 3," or "Process for preparing CCDC semihydrochloride according to Claim 4," respectively, and there is insufficient antecedent basis for this limitation in the claims. The claims relate to a process for preparing a CCDC semihydrochloride compound as defined in claims 2, 3, or 4, respectively. That is, the claims refer to claims 2, 3, or 4, respectively, as a means to define the compound, not the process. The claims have been amended accordingly.

The Examiner stated that claims 19 and 21 recite the limitation "A method of preparing a medicament comprising formulating CCDC semihydrochloride according to claim 2," or "A method of preparing a medicament comprising formulating CCDC semihydrochloride according to claim 1," respectively, and there is insufficient antecedent basis for this limitation in the claims. The claims relate to a method of preparing a medicament comprising a CCDC semihydrochloride as defined in claims 1 or

2, respectively. That is, the claims refer to claims 1 or 2, respectively, as a means to define the compound, not the method. The claims have been amended accordingly.

The Examiner stated that claims 11, 22, 23, and 24 recite the limitation "A process for treating bacteria comprising applying thereto an antibacterial composition containing CCDC semihydrochloride according to claim 1," "A process for treating bacteria comprising applying thereto an antibacterial composition containing CCDC semihydrochloride according to claim 2," "A process for treating bacteria comprising applying thereto an antibacterial composition containing CCDC semihydrochloride according to claim 3," or "A process for treating bacteria comprising applying thereto an antibacterial composition containing CCDC semihydrochloride according to claim 4," respectively, and there is insufficient antecedent basis for this limitation in the claims. The claims relate to a process for treating bacteria comprising applying a composition containing CCDC semihydrochloride as defined in claims 1-4, respectively. That is, the claims refer to claims 1-4, respectively, as a means to define the compound, not the process. The claims have been amended accordingly.

The Examiner stated that the phrase "at least" in claims 4-8 is indefinite. There is no upper limit to the number of carbons contained in the aliphatic alcohols. The claims have been amended to specify the aliphatic alcohols. Please note the phrase "at least" is not present in claim 8. Support for this amendment may be found, for example, on page 8, lines 1-6 of the specification.

It is thus submitted that the claims 1, 4-11, and 13-24 meet the requirements of 35 USC § 112, second paragraph, and reconsideration and withdrawal of the present rejection is respectfully requested.

Rejection Under 35 U.S.C. § 103(a)

In paragraph 3 (page 2-3) of Paper No. 7, the Examiner rejected claims 1-4 and 12 under U.S.C. § 103(a) as unpatentable over Bartel et al., (WO 97/31001; Reference N). Applicants respectfully traverse.

To properly maintain a rejection under 35 U.S.C. § 103, three conditions must be met. First, the prior art must have suggested to those of ordinary skill in the art that they should make the claimed composition or device or carry out the claimed process. Second, the prior art must also have revealed that in so making or carrying out, those of ordinary skill in the art would have a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be adequately founded in the prior art and not in the Applicant's disclosure. Finally, the prior art reference must teach or suggest all the claim limitations. *See In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

The present invention relates to semihydrochloride compounds.

Bartel et al., (WO 97/31001) do not teach or suggest the compounds of the present invention and the requisite reasonable expectation of success is absent. That is, Bartel et al., do not teach or suggest

semihydrochlorides, nor do they teach or suggest how to make semihydrochlorides. It would be readily apparent to one skilled in the art that semihydrochlorides are chemically significant, particularly where functionality of the compound depends on bioavailability. The compounds of the present invention may be used in pharmaceutical compositions for treating bacterial diseases. In order to successfully treat a bacterial disease, the pharmaceutical must be efficacious. However, poor solubility of a pharmaceutical may ultimately led to poor bioavailability and thus, poor efficacy. Therefore, the solubility characteristics of a pharmaceutical compound are important for therapeutic response.

As described in the specification, a CCDC of formula (I), the reference compound, exhibited a solubility of 0.02% (w/w) (page 2), whereas a CCDC hydrochloride of formula (IV) demonstrated a solubility of 2.8% (w/w) (page 4). Surprisingly, the CCDC semihydrochloride exhibited a solubility of 19% (w/w) (page 5); considerably more soluble than the reference compound and the hydrochloride.

Bartel et al., do not teach or suggest semihydrochlorides nor do they teach or suggest that semihydrochlorides would have improved solubility. As such, one skilled in the art would not have been motivated to prepare semihydrochloride compounds with the expectation of producing compounds with improved solubility. Applicants do not see where there is a suggestion to make the compounds of the present invention. Thus, one skilled in the art would not have been motivated to prepare semihydrochlorides with the requisite reasonable expectation of success, that is, producing compounds with improved solubility.

It is therefore respectfully submitted that Bartel et al., (WO 97/31001) fail to teach or suggest the compounds as presently claimed, and that the current invention is novel and nonobvious in view of the prior art references. For the foregoing reasons, Applicants respectfully request reconsideration and withdrawal of the present rejection.

CONCLUSION

For the foregoing reasons, Applicants submit that the claims are in condition for allowance and Applicants respectfully request reexamination of the present application, reconsideration and withdrawal of the present rejections, and entry of the amendments. Should there be any further matter requiring consideration, Examiner Robinson is invited to contact the undersigned counsel.

If there are any further fees due in connection with the filing of the present reply, please charge the fees to undersigned's Deposit Account No. 13-3372. If a fee is required for an extension of time not accounted for, such an extension is requested and the fee should also be charged to undersigned's deposit account.

Respectfully submitted,

Susan M. Pellegrino

October 7, 2002

Susan M. Pellegrino
Reg. No. 48,972

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West Haven, CT 06516-4175
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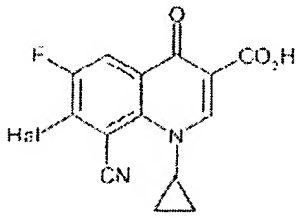
susan.pellegrino.b@bayer.com

Amended Claims (Attorney Docket No. Mo 6341/LeA 33 270)

4. (Twice amended) CCDC semihydrochloride according to Claim 1, obtainable by reacting 7-halogeno-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinoline-carboxylic acid of the formula (II)

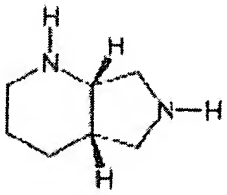


(II),

in which

Hal represents fluorine or chlorine,

and (1S,6S)-2,8-diazabicyclo[4.3.0]nonane of the formula (III)



(III),

optionally in the presence of a base, in one of the following diluents or diluent mixtures:

a) aliphatic alcohols selected from the group consisting of butanol, isobutanol, 2-butanol, tert-butanol, and 1-pentanol,

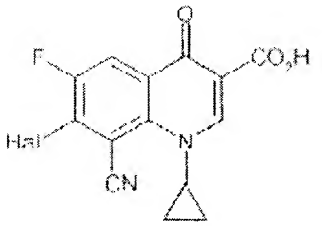
b) mixture of aliphatic alcohols selected from the group consisting of propanol, isopropanol, butanol, isobutanol, 2-butanol, tert-butanol, and 1-pentanol with N-methylpyrrolidone,

c) mixture of propanol and N,N-dimethylformamide,

or

d) mixture of ethanol with N-methyl-pyrrolidone with added tripropylamine, tributylamine, N-ethylmorpholine, N-propylmorpholine and/or N-butylmorpholine base.

5. (Twice amended) A process for preparing CCDC semihydrochloride according to Claim 1, comprising reacting 7-halogeno-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid of the formula (II)

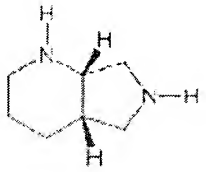


(II).

in which

Hal represents fluorine or represents chlorine

and (1S,6S)-2,8-diazabicyclo[4.3.0]nonane of the formula (III)



(III)

in the presence of a base in one of the following diluents or diluent mixtures:

a) aliphatic alcohols selected from the group consisting of butanol, isobutanol, 2-butanol, tert-butanol, and 1-pentanol,

b) mixture of aliphatic alcohols selected from the group consisting of propanol, isopropanol, butanol, isobutanol, 2-butanol, tert-butanol, and 1-pentanol with N-methylpyrrolidone,

c) mixture of propanol and N,N-dimethylformamide,

or

d) mixture of ethanol with N-methyl-pyrrolidone with added tripropylamine, tributylamine, N-ethylmorpholine, N-propylmorpholine and/or N-butylmorpholine base.

6. (Twice amended) A process for preparing CCDC semihydrochloride according to Claim 5, wherein the diluent used is an aliphatic alcohol selected from the group consisting of butanol, isobutanol, 2-butanol, tert-butanol, and 1-pentanol or that an aliphatic alcohol selected from the group consisting of ethanol, propanol, isopropanol, butanol, isobutanol, 2-butanol, tert-butanol, and 1-pentanol is used as component of a diluent mixture.

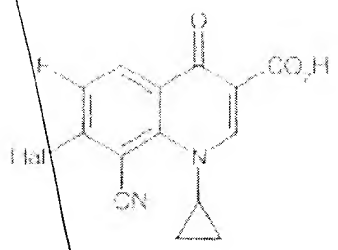
7. (Twice amended) A process for preparing CCDC semihydrochloride according to Claim 5, wherein if an aliphatic alcohol selected from the group consisting of propanol, isopropanol, butanol, isobutanol, 2-butanol, tert-butanol, and 1-pentanol is used as component of a diluent mixture, N-methyl-pyrrolidone is simultaneously employed as a further diluent in a ratio of from 1 to 1 to 3 to 1.

9. (Twice amended) A pharmaceutical composition comprising, in addition to customary auxiliaries and excipients, CCDC semihydrochloride according to Claim 1.

10. (Twice amended) A method of preparing a pharmaceutical composition comprising formulating CCDC semihydrochloride according to Claim 1.

11. (Twice amended) A process for treating bacteria comprising applying thereto an antibacterial composition containing CCDC semihydrochloride as defined in Claim 1.

13. (Amended) A process for preparing a CCDC semihydrochloride as defined in Claim 2, characterized in that 7-halogeno-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid of the formula (II)

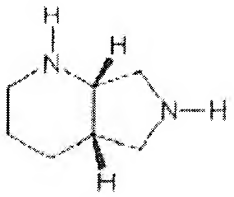


(II),

in which

Hal represents fluorine or represents chlorine

and (1S, 6S)-2,8-diazabicyclo[4.3.0]nonane of the formula (III)



(III)

are reacted in the presence of a base in one of the following diluents or diluent mixtures:

a) aliphatic alcohols having at least four carbon atoms,

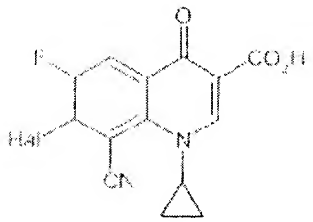
b) mixture of aliphatic alcohols having at least three carbon atoms with N-methylpyrrolidone,

c) mixture of propanol and N,N-dimethylformamide,

or

d) mixture of ethanol with N-methyl-pyrrolidone with added tripropylamine, tributylamine, N-ethylmorpholine, N-propylmorpholine and/or N-butylmorpholine base.

14. (Amended) A process for preparing a CCDC semihydrochloride as defined in Claim 3, characterized in that 7-halogeno-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid of the formula (II)



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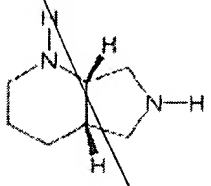


(III)

are reacted in the presence of a base in one of the following diluents or diluent mixtures:

a) aliphatic alcohols having at least four carbon atoms,

b) mixture of aliphatic alcohols having at least three carbon atoms with N-methylpyrrolidone,

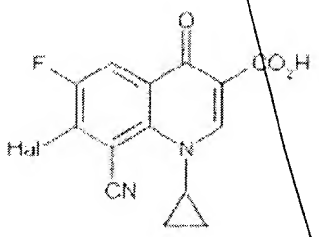
c) mixture of propanol and N,N-dimethylformamide,

or

d) mixture of ethanol with N-methyl-pyrrolidone with added tripropylamine, tributylamine,

N-ethylmorpholine, N-propylmorpholine and/or N-butylmorpholine base.

15. (Amended) A process for preparing a CCDC semihydrochloride as defined in Claim 4, characterized in that 7-halogeno-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid of the formula (II)



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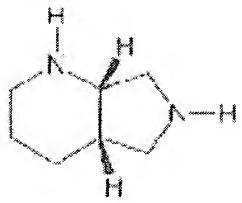


(III)

are reacted in the presence of a base in one of the following diluents or diluent mixtures:

a) aliphatic alcohols having at least four carbon atoms,

b) mixture of aliphatic alcohols having at least three carbon atoms with N-methylpyrrolidone,

c) mixture of propanol and N,N-dimethylformamide,

or

d) mixture of ethanol with N-methyl-pyrrolidone with added tripropylamine, tributylamine, N-ethylmorpholine, N-propylmorpholine and/or N-butylmorpholine base.

16. (Amended) A pharmaceutical composition comprising, in addition to customary auxiliaries and excipients, CCDC semihydrochloride according to Claim 2.

17. (Amended) A pharmaceutical composition comprising, in addition to customary auxiliaries and excipients, CCDC semihydrochloride according to Claim 3.

18. (Amended) A pharmaceutical composition comprising, in addition to customary auxiliaries and excipients, CCDC semihydrochloride according to Claim 4.

19. (Amended) A method of preparing a pharmaceutical composition comprising formulating CCDC semihydrochloride as defined in Claim 2.

20. (Amended) A method of preparing a pharmaceutical composition comprising formulating CCDC semihydrochloride as defined in Claim 2.

21. (Amended) A method of preparing pharmaceutical composition comprising formulating CCDC semihydrochloride as defined in Claim 1.

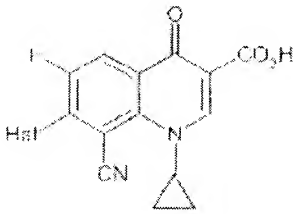
22. (Amended) A process for treating bacteria comprising applying thereto an antibacterial composition containing CCDC semihydrochloride as defined in Claim 2.

23. (Amended) A process for treating bacteria comprising applying thereto an antibacterial composition containing CCDC semihydrochloride as defined in Claim 3.

24. (Amended) A process for treating bacteria comprising applying thereto an antibacterial composition containing CCDC semihydrochloride as defined in Claim 4.

Amendments to the Claims (Attorney Docket No. Mo 6341/LeA 33 270)
Version with Markings to Show Changes to Specification

4. (Twice amended) CCDC semihydrochloride according to Claim 1, obtainable by reacting 7-halogeno-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinoline-carboxylic acid of the formula (II)



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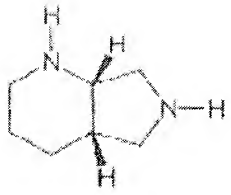


(III),

optionally in the presence of a base, in one of the following diluents or diluent mixtures:

a) aliphatic alcohols [having at least four carbon atoms] <u>selected from the group consisting of butanol, isobutanol, 2-butanol, tert-butanol, and 1-pentanol,</u>

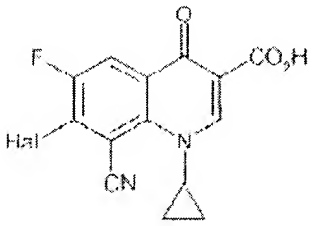
b) mixture of aliphatic alcohols [having at least three carbon atoms] <u>selected from the group consisting of propanol, isopropanol, butanol, isobutanol, 2-butanol, tert-butanol, and 1-pentanol</u> with N-methylpyrrolidone,

c) mixture of propanol and N,N-dimethylformamide,

or

d) mixture of ethanol with N-methyl-pyrrolidone with added tripropylamine, tributylamine, N-ethylmorpholine, N-propylmorpholine and/or N-butylmorpholine base.

5. (Twice amended) A [P]process for preparing CCDC semihydrochloride according to Claim 1, comprising reacting 7-halogeno-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid of the formula (II)



(II).

in which

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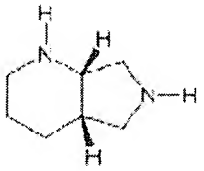
and (1S,6S)-2,8-diazabicyclo[4.3.0]nonane of the formula (III)



(III)

in the presence of a base in one of the following diluents or diluent mixtures:

a) aliphatic alcohols [having at least four carbon atoms] selected from the group consisting of butanol, isobutanol, 2-butanol, tert-butanol, and 1-pentanol,

b) mixture of aliphatic alcohols [having at least three carbon atoms] selected from the group consisting of propanol, isopropanol, butanol, isobutanol, 2-butanol, tert-butanol,

and 1-pentanol with N-methylpyrrolidone,

c) mixture of propanol and N,N-dimethylformamide,

or

d) mixture of ethanol with N-methyl-pyrrolidone with added tripropylamine, tributylamine, N-ethylmorpholine, N-propylmorpholine and/or N-butylmorpholine base.

6. (Twice amended) A [P]process for preparing CCDC semihydrochloride according to Claim 5, wherein the diluent used is an aliphatic alcohol [having at least 4 carbon atoms] selected from the group consisting of butanol, isobutanol, 2-butanol, tert-butanol, and 1-pentanol or that an aliphatic alcohol [having at least two carbon atoms] selected from the group consisting of ethanol, propanol, isopropanol, butanol, isobutanol, 2-butanol, tert-butanol, and 1-pentanol is used as component of a diluent mixture.

7. (Twice amended) A [P]process for preparing CCDC semihydrochloride according to Claim 5, wherein if an aliphatic alcohol [having at least 3 carbon atoms] selected from the group consisting of propanol, isopropanol, butanol, isobutanol, 2-butanol, tert-butanol, and 1-pentanol is used as component of a diluent mixture, N-methyl-pyrrolidone is simultaneously employed as a further diluent in a ratio of from 1 to 1 to 3 to 1.

9. (Twice amended) [Medicament, characterized in that it] A pharmaceutical composition [comprises] comprising, in addition to customary auxiliaries and excipients, CCDC semihydrochloride according to Claim 1.

10. (Twice amended) A method of preparing a [medicament] pharmaceutical composition comprising formulating CCDC semihydrochloride according to Claim 1.

11. (Twice amended) A process for treating bacteria comprising applying thereto an antibacterial composition containing CCDC semihydrochloride [according to] as defined in Claim 1.

13. (Amended) A [P]process for preparing a CCDC semihydrochloride [according to] as defined in Claim 2, characterized in that 7-halogeno-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-

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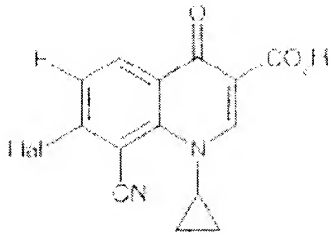
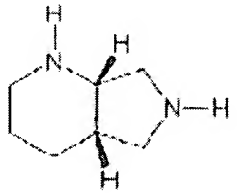


(II)

in which

Hal represents fluorine or represents chlorine

and (1S, 6S)-2,8-diazabicyclo[4.3.0]nonane of the formula (III)



(III)

are reacted in the presence of a base in one of the following diluents or diluent mixtures:

a) aliphatic alcohols having at least four carbon atoms,

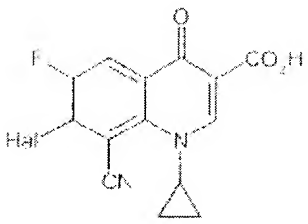
b) mixture of aliphatic alcohols having at least three carbon atoms with N-methylpyrrolidone,

c) mixture of propanol and N,N-dimethylformamide,

or

d) mixture of ethanol with N-methyl-pyrrolidone with added tripropylamine, tributylamine, N-ethylmorpholine, N-propylmorpholine and/or N-butylmorpholine base.

14. (Amended) A [P]process for preparing a CCDC semihydrochloride [according to] as defined in Claim 3, characterized in that 7-halogeno-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid of the formula (II)



(II),

in which

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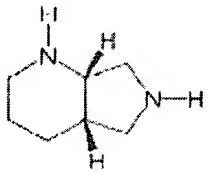
and (1S,6S)-2,8-diazabicyclo[4.3.0]nonane of the formula (III)



(III)

are reacted in the presence of a base in one of the following diluents or diluent mixtures:

a) aliphatic alcohols having at least four carbon atoms,

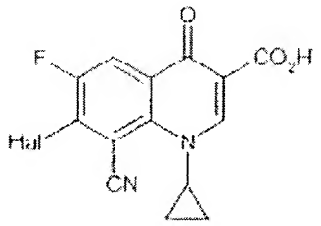
b) mixture of aliphatic alcohols having at least three carbon atoms with N-methylpyrrolidone,

c) mixture of propanol and N,N-dimethylformamide,

or

d) mixture of ethanol with N-methyl-pyrrolidone with added tripropylamine, tributylamine, N-ethylmorpholine, N-propylmorpholine and/or N-butylmorpholine base.

15. (Amended) A [P]process for preparing a CCDC semihydrochloride [according to] as defined in Claim 4, characterized in that 7-halogeno-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid of the formula (II)

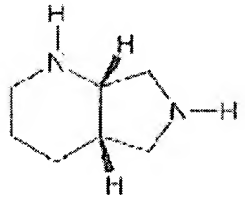


(II),

in which

Hal represents fluorine or represents chlorine

and (1 S,6S)-2,8-diazabicyclo[4.3.0]nonane of the formula (III)



(III)

are reacted in the presence of a base in one of the following diluents or diluent mixtures:

a) aliphatic alcohols having at least four carbon atoms,

b) mixture of aliphatic alcohols having at least three carbon atoms with N-

methylpyrrolidone,

c) mixture of propanol and N,N-dimethylformamide,

or

d) mixture of ethanol with N-methyl-pyrrolidone with added tripropylamine, tributylamine, N-ethylmorpholine, N-propylmorpholine and/or N-butylmorpholine base.

16. (Amended) [Medicament, characterized in that it] A pharmaceutical composition [comprises] comprising, in addition to customary auxiliaries and excipients, CCDC semihydrochloride according to Claim 2.

17. (Amended) [Medicament, characterized in that it] A pharmaceutical composition [comprises] comprising, in addition to customary auxiliaries and excipients, CCDC semihydrochloride according to Claim 3.

18. (Amended) [Medicament, characterized in that it] A pharmaceutical composition [comprises] comprising, in addition to customary auxiliaries and excipients, CCDC semihydrochloride according to Claim 4.

19. (Amended) A method of preparing a [medicament] pharmaceutical composition comprising formulating CCDC semihydrochloride [according to] as defined in Claim 2.

20. (Amended) A method of preparing a [medicament] pharmaceutical composition comprising formulating CCDC semihydrochloride [according to] as defined in Claim 2.

21. (Amended) A method of preparing [medicament] pharmaceutical composition comprising formulating CCDC semihydrochloride [according to] as defined in Claim 1.

22. (Amended) A process for treating bacteria comprising applying thereto an antibacterial composition containing CCDC semihydrochloride [according to] as defined in Claim 2.

23. (Amended) A process for treating bacteria comprising applying thereto an antibacterial

composition containing CCDC semihydrochloride [according to] as defined in Claim 3.

24. (Amended) A process for treating bacteria comprising applying thereto an antibacterial composition containing CCDC semihydrochloride [according to] as defined in Claim 4.